Number 153

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WP+ 99U CRP-001-CPIII 01/25/90

Part 2
#5

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Rueger et al.	Examiner:	
Serial No.:	422,699	Group Art Unit:	153 ~~158~~
Filed:	October 17, 1989	Attorney Docket:	CRP-001-CP3
Title:	OSTEOGENIC DEVICES		

Honorable Commissioner of Patents and Trademarks
Washington, DC 20231

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Honorable Commissioner of Patents and Trademarks, Washington, DC 20231 on the date set forth below.

1/25/90
Date of Signature and of Mail Deposit

By Edmund R. Pitcher
Edmund R. Pitcher
Registration No. 27,829
Attorney for Applicants

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SUPPLEMENTAL INFORMATION
DISCLOSURE STATEMENT

Dear Sir:

Applicants and their attorney hereby make of record the following additional publications found in PCT Search Reports on W089/01453 and WO89/01469.

A PTO Form 1449 and copies of the PCT Search Reports accompany this statement. Copies of the documents accompany the Supplemental Information Disclosure Statement submitted for copending U.S. Patent Application No. 315,342.

U.S. Patent No. 4,394,370, Jefferies, "Bone Graft Material for Osseous Defects and Method of Making Same" (filed September 21, 1981), issued July 19, 1983 is understood to disclose a composition for repairing osseous defects. The composition comprises reconsituted collagen, preferably crosslinked, and demineralized bone particles or bone morphogenic protein.

EP 0,182,483 is understood to claim a composition suitable for inductive bone implants comprising nonfibrillar, atelopeptide collagen.

U.S. Patent No. 4,563,489, Urist, "Biodegradable Organic Polymer Delivery System for Bone Morphogenetic Protein" (filed February 10, 1984), issued January 7, 1986 is understood to relate to a polylactic acid polymer delivery system for bone morphogenic protein.

Colowick et al., Methods in Enzymology 146:294-312 (1987) is understood to describe a method of preparing bone morphogenic protein and polypeptide fragments.

WO86/00526, Caplan et al., "Process for Adapting Soluble Bone Protein for Use in Stimulating Osteoinduction", filed July 5, 1985, published January 30, 1986 is understood to disclose carriers for the time-dependent release of soluble bone protein. The carrier comprises fibrin clots and demineralized, extracted bone chips that are crosslinked or surface-coated with gelatin and/or fibrin.

WO85/05274, Oliver et al., "Implant Tissue", filed May 24, 1985, published December 5, 1985, is understood to disclose a collagenous fibrous tissue preparation for repair of cutaneous wounds and soft tissue injuries. The tissue preparation, preferably in sheet form, is produced by treatment of the tissue with a polyisocyanate.

EPO 169,016, Seyedin, "Polypeptide Cartilage-inducing Factors Found in Bone", filed July 8, 1985, published January 22, 1986, is understood to disclose two polypeptide factors isolated from bone having chondrogenic and TGF-ß activity.

Olson et al., Analyt. Biochem. 146:232-237 (1985) is understood to describe the deglycosylation of chondroitin sulfate proteoglycan with hydrogen fluoride in pyridine.

Seyedin et al., J. Cell Biol. 97:1950-1953 (1983) is understood to describe an in vitro system developed to study the onset of chondrogenesis.

Simpson, Trends Biochem. Sci. 9:527-530 (1984) is understood to review the role of growth factors in both bone resorption and formation, as understood to date.

EPO 128,041, Baylink, "Polypeptides Exhibiting Skeletal Growth Factor Activity", filed June 5, 1984, published December 12, 1984 is understood to describe three polypeptide compositions exhibiting skeletal growth factor activity.

Maugh, Science 217:819 (1982) is understood to announce the isolation of human skeletal growth factor and distinguishes it from osteogenic (bone morphogenic) protein.

Padgett et al., Nature 325:81-84 (1987) is understood to disclose the cDNA sequence of a drosophila development gene (DPP-C) and its homology to the related genes of the TGF-ß gene family.

U.S. Patent No. 4,563,350, Nathan et al., "Inductive Collagen Based Bone Repair Preparations" (filed October 24, 1984), issued January 7, 1986 is understood to disclose a composition suitable for inductive bone implants, comprising a purified form of osteogenic factor mixed with a carrier having a percentage of non-fibrillar collagen.

Respectfully submitted,

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January 25, 1990

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

GROUP 150

Applicant: Rueger et al.

Examiner:

Serial No.: 422,699

Group Art Unit: ~~158~~ 153

Filed: October 17, 1989

Attorney Docket: CRP-001CP3

Title: OSTEOGENIC PROTEIN

#5

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INFORMATION DISCLOSURE STATEMENT

Dear Sir:

In accordance with 37 CFR 1.97, Applicants and their attorney hereby make of record the publications which were brought to the attention of the Patent and Trademark Office in relation to the parent case, Serial No. 315,342, filed February 23, 1989. In addition, Applicants and their attorney make of record WO 89/09605, WO 89/10409, U.S. 4,877,864 and Lyons et al. (1989).

A PTO Form 1449 and copies of the additional documents accompany the statement.

U.S. 4,294,753 is understood to relate to the process of separating bone morphogenetic protein from demineralized bone tissue.

U.S. 4,434,094 is understood to relate to partially purified osteogenic factor and a process for preparing it from demineralized bone.

U.S. 4,455,256 is understood to relate to the characterization of bone morphogenic protein prepared from demineralized bone.

PCT WO 88/00205 is understood to relate to four purified human and bovine cartilage and bone inductive factors and their production by recombinant techniques.

EP 0,148,155 is understood to relate to a protein extracted from demineralized bone matrix exhibiting bone-inducing activity, and a method for its isolation and purification.

EP 0,212,474 is understood to relate to the production and isolation of bone morphogenic peptide agents by recombinant means.

Canalis et al. (1980) is understood to relate to the stimulation of DNA and collagen synthesis by a growth factor in cultured fetal rat calvari.

Glowacki et al. (1981) is understood to relate to the application of demineralized bone implants for cranio-maxillofacial reconstruction involving osteogenesis.

Reddi (1981) is understood to relate to a review of the cell biology and biochemistry of endochondral bone development, including a discussion of the developmental cascade of bone resorption and remodeling.

Sampath et al. (1981) is understood to relate to the dissociative extraction and reconstitution of extracellular matrix components involved in local bone differentiation.

Farley et al. (1982) is understood to relate to human skeletal growth factor and characterization of its mutogenic effect on bone cells in vitro.

Urist et al. (1983) is understood to relate to the physical and biological characterization of several human bone morphogenetic protein extracted from demineralized, gelatinized cortical bone matrix.

Sampath et al. (1983) is understood to relate to the bone inductive proteins from human, monkey, bovine, and rat extracellular matrix, and to a comparison of their biochemical and enzymatic characteristics.

Urist et al. (1984) is understood to relate to the differentiation of cartilage into bone by induction with an aggregate of ß-tricalcium phosphate and bone morphogenetic protein.

Urist et al., II (1984) is understood to relate to the purification and characterization of several bovine bone morphogenetic proteins by hydroxyapatite chromatography.

Reddi (1985) is understood to relate to the cascade of implant-stimulated interface reactions which occur during collagenous bone matrix-induced bone formation.

Seyedin et al. (1985) is understood to relate to the purification of two cartilage-inducing factors from bovine demineralized bone including dissociative extraction, gel filtration, cation exchange chromatography, and reverse phase HPLC. It also is understood to relate to the characterization of these cartilage-inducing factors.

Klausner (1985) is understood to relate to the isolation of two cartilage-inducing factors, and to an in vitro assay for chondrogenetic activity.

Centrella et al. (1985) is understood to relate to the purification and characterization of transforming and nontransforming growth factors present in medium conditioned by fetal rat calvariae.

Sampath et al. (1985) is understood to relate to a review of the cellular and biochemical events associated with matrix-induced endochondral bone formation, and to the role of extracellular matrix components in these events.

Weeks et al. (1987) is understood to relate to the characterization and localization of a maternal mRNA from Xenopus eggs which encodes a member of the transforming growth factor-B family of proteins.

Sampath et al. (1987) is understood to relate to the isolation and characterization of an extracellular, matrix-associated bone inductive protein by heparin affinity chromatography.

LeGendre et al. (1988) is understood to relate to the use of Immobilon transfer membranes on to which proteins have been electrophoretically transferred for direct protein sequencing in a gas phase sequencer.

Wang et al. (1988) is understood to relate to the isolation and characterization of factors from bovine bone that induce cartilage and ectopic bone formation in vivo.

Wozney et al. (1988) is understood to relate to the cloning and identification of three proteins involved in in vivo cartilage formation.

Wang et al., II (1988) is understood to relate to the isolation and characterization of factors from demineralized bone that induce cartilage and new bone formation in vivo.

Wozney et al., II (1988) is understood to relate to the cloning and identification of three proteins involved in *in vivo* cartilage formation.

WO 86/00526 is understood to claim a method for treating implants to enhance or stimulate cartilage and/or bone formation.

Jefferies (1983) is understood to relate to an osteogenic collagen conjugate material, particularly in the form of a sponge, and a process for making this material. The material is comprised primarily of reconstituted collagen.

EP 0,182,483 is understood to claim a composition suitable for inductive bone implants comprising nonfibrillar, atelopeptide collagen.

Urist (1986) is understood to relate to a polylactic acid polymer delivery system for bone morphogenic protein.

Colowick et al., *Methods in Enzymology* 146:294-312 (1987) is understood to describe a method of preparing bone morphogenic protein and polypeptide fragments.

PCT/US89/09605 is understood to disclose a polypeptide sequence isolated from bone having osteogenic activity at non-bony sites in the presence of TGF-ß.

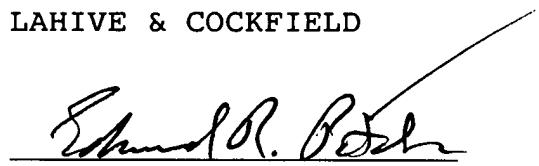
PCT/WO89/10409 is understood to disclose a polypeptide sequence isolated from bone (BMP-3), and a DNA sequence encoding it. The protein is purported to have osteogenic activity.

U.S. Patent No. 4,877,864, Wang et al., "Osteoinductive Factors", filed March 26, 1987, is understood to claim an amino acid sequence isolated from bone (BMP-1) and a DNA sequence encoding it. This protein is purported to have osteogenic activity.

Lyons et al., Proc. Natl. Acad. Sci. USA 86:4554-4558 (1989) is understood to relate to a sequence comparison of Vgr-1 DNA with that of other genes thought to be in the TGF-ß superfamily.

Respectfully submitted,

LAHIVE & COCKFIELD



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